

### REMARKS

Claims 15, 16, and 36-60 are pending in the application. Claims 15, 16, 37, 39, and 56 are amended. Support for the amendments can be found throughout the specification and claims as originally filed. For example, support for amended claims 15 and 56 can be found, *e.g.*, at page 5, lines 11-14, and support for amended claim 39, can be found, *e.g.*, at page 20, line 24. The amendments to the specification are to insert a corrected sequence listing and sequence identifiers, and to address objections raised by the Examiner. Support for the amendments can be found in Figures 2-5 as originally filed, and at page 31, lines 23-27, and page 32, lines 10-24. No new matter is added by the amendments.

Applicants respectfully request that the Examiner initial Ref. No. 9 on the form 1449 submitted December 10, 2001. For the Examiner's convenience, a copy of the reference (Thanker *et al.* "Design and Synthesis of Novel Selectin Inhibitors." Book of Abstracts, 218<sup>th</sup> ACS National Meeting, New Orleans, August 22-26, 1999 (Abstract)) is enclosed as Exhibit A. Applicants note that this 1-page reference is scanned into PAIR at the website of the U.S. Patent and Trademark Office as the last page of the reference Somers *et al.*, Cell 103:467-479, 2000, also submitted on December 10, 2001.

### Objections

*Drawings.* The Examiner objected to the drawings "because Figures 2-5 should have some sort of identifier at the start of each table detailing the contents of the .pdb coordinates." Office Action at page 3. Applicants note that the start of each table does have identifiers that describe the contents of the tables. In each of Figures 2-5, the columns describing atom type, amino acid residue, the x, y and z coordinates, occupancy value, B value and molecule identifier are labeled accordingly. These labels are the norm for PDB coordinate tables, and the headings are even defined in the figure legends. The Examiner also states that each table should include a SEQ ID NO, the space group, the unit cell parameters and the number of molecules per asymmetric unit. Applicants have added this information to the figure legends in the Brief

Description of the Drawings and submit that this amendment is sufficient to adequately describe the tables. Applicants respectfully request that the objection to the drawings be withdrawn.

*Compliance with Sequence Rules.* A substitute sequence listing is enclosed. The specification has been amended to insert SEQ ID NOs in the brief description of the drawings.

*Specification.* The Brief Description of the Drawings has been amended to clarify the number of molecules per asymmetric unit in Figures 2-5.

*Claims.* Claim 39 was amended to correct a typographical error, as suggested by the Examiner.

#### 35 U.S.C. § 101, Utility

The Examiner rejected claims 15, 16, and 36-60 under 35 U.S.C. § 101 for lack of utility. The Examiner states that "in the absence of a disclosed correlation between the interaction of an agent with P-selectin and some sort of modulation (*e.g.*, activation, inhibition, etc.) resulting from said interaction...merely identifying compounds which may interact with protein P-selectin LE is not a specific, substantial, and credible utility." Office Action at page 8. Applicants disagree.

The Trilateral Project WM4 (hereafter "the Trilateral Report") at page 24, in the analysis of Case 6, states that the claims comply with the utility requirement

if the specification teaches that the binding compounds may be used to either stimulate activity of protein P to reduce blood pressure, or... inhibit the activity of protein P to cause an increase in blood pressure. An assertion of either or both of these uses for a protein P binding compound that is credible to one skilled in the art would be accepted as a specific, substantial and credible utility.

Indeed, Applicants' specification includes an assertion that small molecules or agents "which inhibit or otherwise interfere with the selectin-mediated cellular rolling of leukocytes

over vascular tissue” can be used for the treatment of asthma and psoriasis. Specification at page 10, lines 22-25. One of skill in the art would find this assertion credible, at least because the specification teaches that selectins are responsible for, *inter alia*, early adhesion events in the recruitment of leukocytes into sites of inflammation. See, Specification at page 1, lines 18-20. Since the assertion of the uses for a P-selectin LE binding compound is credible to one skilled in the art, and as stated in the Trilateral Report (and as quoted above), the assertion should be accepted as a specific, substantial, and credible utility.

The Examiner states that “the specification fails to specifically detail the specific utility for the compounds that are being identified in the method claims and merely skirts around the issue by identifying *potential* uses of the compounds; however, these potential uses may constitute false prophecies.” Office Action at page 7 (emphasis in original). Applicants note that MPEP § 2107(II)(B)(1) (“Guidelines for Examination of Applications for Compliance with the Utility Requirement”, hereafter “the Utility Guidelines”) clearly states that a rejection based on lack of utility should not be imposed “[i]f the applicant has asserted that the claimed invention is useful for any particular practical purpose (*i.e.*, it has a ‘specific and substantial utility’) and the assertion would be considered credible by a person of ordinary skill in the art.” (emphasis added). Applicants have satisfied this requirement, at least because Applicants asserted at page 10, lines 22-25, that small molecules or agents “which inhibit or otherwise interfere with the selectin-mediated cellular rolling of leukocytes over vascular tissue” can be used for the treatment of asthma and psoriasis. As required by the Utility Guidelines, this is an assertion that the compounds to be identified by the claimed methods have a particular practical purpose. Further, Applicants’ assertion would be considered credible by a person of ordinary skill in the art at least because selectins are known to be involved in early adhesion events in the recruitment of leukocytes into sites of inflammation. See, Specification at page 1, lines 18-20. Thus Applicants’ claims have a specific, substantial and credible utility.

In view of the above arguments, Applicants request reconsideration and withdrawal of the rejection of claims 15, 16, and 36-60 under 35 U.S.C. § 101 for lack of utility.

Since the claims are supported by a specific, substantial and credible asserted utility, and for at least the reasons described above, one having skill in the art would certainly know how to use the claimed invention. Applicants therefore also request withdrawal of the rejection under 35 U.S.C. § 112, first paragraph.

35 U.S.C. § 112, second paragraph

The Examiner rejected claims 15, 16, and 36-60 under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph as being indefinite. The claims are deemed indefinite for the recitation "employing said three-dimensional model to design or select an agent" as it is unclear as to how the 3-D structure is "employed" in the design or selection. Applicants maintain that it would be clear from the specification how to "employ" (*i.e.*, to use) the three-dimensional model to design or select an agent. Support for this language is found, *e.g.*, at page 22, lines 13-30.

The Examiner rejected claims 15, 16, and 36-60 as being indefinite because the metes and bounds of the term "relative structural coordinates" are not defined in the claims or in the specification and it is unclear to those of skill in the art. Applicants disagree. The term "relative structural coordinates" is well-known to those skilled in the art of protein crystallography. Support for the term relative as used in the context of the claims can be found in the specification at least at page 15, lines 16-19. The Examiner states "there is no way to determine the scope to which patentability is sought." Office Action at page 9. Applicants disagree. Independent claims 15 and 56 are specifically directed to a method that includes generating a three dimensional model of P-selectin LE using the relative structural coordinates according to Figures 2, 3 or 5,  $\pm$  a root mean square deviation from the backbone atoms of said amino acids of not more than 1.5Å. The claimed scope is supported by the specification.

The Examiner asserted that claim 16 omits essential steps, referencing M.P.E.P. § 2172.01. However, this section of the M.P.E.P. relates to circumstances where an Applicant discloses that certain subject matter is critical. Applicants made no such disclosure in the present application. Applicants therefore maintain that claim 16 does not omit essential steps.

The amendment to claim 37 is believed to overcome the rejection under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph.

In view of the foregoing, Applicants request reconsideration and withdrawal of the rejection of claims 15, 16, and 36-60 under 35 U.S.C. § 112, second paragraph.

35 U.S.C. § 103

Claims 15 and 36-55 were rejected under 35 U.S.C. § 103 as being unpatentable over Revelle *et al.* (*Jour. Biol. Chem.* 271:16160-16170, 1996) in view of Morris *et al.* (*J. of Comp. Aided Molec. Des.* 10:293-304, 1996) in view of *In re Gulack* and *In re Ngai*.

The Examiner states at page 12 of the Office Action, that

All claim limitations concerning the machine readable data comprising structure coordinate data of Figures 2, 3, and 5 are given no patentable weight as it is considered to be non-functional descriptive material. As such, the instant claims are considered to be limited to a method of using a known computer program to identify agents that interact with P-selectin by inputting the three-dimensional structural coordinates into said computer program, and analyzing the output by visual/mental interpretation.

Applicants do not concede that the structural coordinates of claims 2, 3 and 5 are non-functional descriptive material. However, to expedite prosecution, Applicants have added a step of providing a crystal comprising a P-selectin LE to independent claims 15 and 56. In view of the amendment, the claims cannot be said to be "limited to a method of using a known computer program to identify agents." Revelle *et al.* does not teach or suggest the three-dimensional structure of P selectin LE, or the *in silico* design and identification of inhibitors of P-selectin, and the teachings of Morris *et al.*, *In re Gulack* and *In re Ngai* do not make up for this deficiency.

In view of the amendment to the claims, Applicants respectfully request withdrawal of the rejection of claims 15 and 36-55 under 35 U.S.C. § 103 as being unpatentable over Revelle *et al.* in view of Morris *et al.* in view of *In re Gulack* and *In re Ngai*.

Claims 15, 16 and 36-60 were rejected under 35 U.S.C. § 103 as being unpatentable over Graves *et al.* in view of Morris *et al.* and as evidenced by the root-mean square deviation (rmsd) comparisons of the three-dimensional structural coordinates of Figures 2, 3 and 5 with that of the three-dimensional structural coordinates of Graves *et al.* (pdb accession code:1ESL). Graves *et al.* teaches the X-ray crystal structure of E-selectin LE, but Graves *et al.* does not teach the three dimensional structure of P-selectin LE and methods of identifying agents that interact with P-selectin LE.

As amended, independent claims 15 and 56 include a step of providing a crystal comprising a P-selectin LE. There is no suggestion of how one would accomplish this step in Graves, even in view of Morris. As explained by the United States Court of Appeals for the Federal Circuit in Beckman Instruments, Inc. v. LKB Produkter AB, 892 F.2d 1547, 1551 (Fed. Cir. 1989): “[i]n order for the prior art to render a claimed apparatus or method obvious, the prior art must enable one skilled in the art to make and use the apparatus or method.”

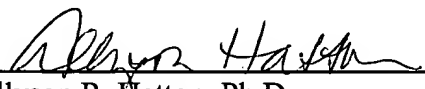
In view of the amendment to the claims, Applicants request reconsideration and withdrawal of the rejection of claims 15, 16, and 36-60 under 35 U.S.C. § 103.

Applicants believe the claims are in condition for allowance, which action is requested.

Please apply the \$120 fee for the One-Month Petition for Extension of Time, and any other necessary charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 16163-004001.

Respectfully submitted,

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